

### **REMARKS**

Upon entry of the amendment, claims 2, 4 to 11, and 53 to 55 will be pending. A marked version of claims 54 and 55 showing the amendments is attached as Exhibit A.

#### **A. Regarding the Amendments**

Claims 43 to 52 are cancelled herein without disclaimer, and without prejudice to Applicants' pursuing prosecution of subject matter encompassed within one or more of the claims in an application claiming the benefit of priority of the subject application.

Claims 54 and 55 have been amended to correct the dependency. As such, the amendments merely address a formality, and do not add new matter.

#### **B. Rejection Under 35 U.S.C. § 101**

The rejection of claims 2, 4 to 11, and 43 to 55 under 35 U.S.C. § 101 as allegedly lacking utility is respectfully traversed. It is noted that claims 43 to 52 have been cancelled herein.

It is stated in the Office Action that the claimed subject matter, directed to a polynucleotide encoding a GDF-16 polypeptide, is not supported in the specification by either a specific and substantial credible asserted utility or a well-established utility. In particular, it is alleged that no activity or disorder known to be associated with the encoded GDF-16 polypeptide is disclosed, and that further research would be required to identify such an activity or disorder, for example, a disease in which GDF-16 activity could be beneficially affected or which its presence would be diagnostic.

Applicants respectfully submit, however, that the specification clearly discloses specific and substantial credible utilities for a GDF-16 protein and encoding polynucleotide. For example, the specification discloses that GDF-16 can have cell growth and differentiation activity and can be useful as a marker for a cell proliferative disorder (see page 3, lines 2-4; page 4, lines 1-8). The specification also discloses that a GDF-16 polynucleotide, as well as reagents specific for GDF-16 expression, can be useful for diagnosing and treating a cell

proliferative disorder associated with GDF-16 expression (see, page 19, lines 3-10), for example, a malignant cell proliferative disorder (see page 15, lines 17-24). More specifically, the specification discloses that a GDF-16 polynucleotide can be utilized in detecting and diagnosing a cell proliferative disorder by detecting a level of GDF-16 expression that is altered as compared with that of a normal cell (page 19, lines 3-10).

It is submitted that the disclosure in the specification is credible, as evidenced by reports that proteins similar to GDF-16, and encoded by homologous polynucleotides, can be expressed in a tissue specific manner and indicative of malignant cell disorders. For example, the Tabibzadeh et al. reference, which is of record in this case, describes tumor specific expression of the TGF $\beta$ -4 (endometrial bleeding associated factor; "ebaf") gene, including increased levels of ebaf in mucinous adenocarcinoma cells of the colon or ovaries, or in adenocarcinoma cells of the testes compared to a non-carcinoma cell (see U.S. Pat. No. 5,916,751; Abstract). As the Examiner noted in Paper No. 17, the polynucleotide sequence described in the '751 patent contains a region of 303 nucleotides that is 92% homologous to SEQ ID NO: 1 of the subject application. As such, Applicants submit that one skilled in the art, viewing the subject application, and having knowledge of the '751 patent, reasonably would have known that a polynucleotide encoding GDF-16 can be useful in the detection and early diagnosis of a malignant cell proliferative disorder. Accordingly, it is submitted that the specification discloses specific and substantial utilities for a GDF-16 polynucleotide, including, for example, as a reagent (or a target for a reagent) that can be diagnostic of a malignant cell proliferative disorder, and that the skilled artisan would have known that such a utility is credible because a similar utility was known for a related polynucleotide.

In summary, the specification clearly discloses specific and substantial utilities for a polynucleotide encoding GDF-16, and that the disclosed utilities are credible as evidenced by knowledge in the art of related polynucleotides. Accordingly, it is respectfully requested that the rejection of the claims under 35 U.S.C. § 101 as allegedly lacking utility be removed.

**C. Rejection Under 35 U.S.C. § 112**

The rejection of claims 2, 4 to 11, and 43 to 55 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement is respectfully traversed.

It is stated in the Office Action that the claimed polynucleotides are not supported by either a specific and substantial credible utility or a well established utility and, therefore, that one skilled in the art would not have known how to use the claimed polynucleotides. However, for the reasons set forth above, it is submitted that the specification discloses a specific and substantial credible utility. It is further submitted that, in view of the specification, the skilled artisan would have known how to use a GDF-16 polynucleotide as claimed, for example, as a diagnostic reagent, without undue experimentation. Accordingly, it is respectfully requested that this rejection of the claims under 35 U.S.C. § 112, first paragraph, be removed.

The rejection of claims 43 and 47 to 52 under 35 U.S.C. § 112, first paragraph, as allegedly lacking an adequate written description are respectfully traversed.

It is alleged in the Office Action that there is no support in the specification for fragments, or sequences comprising fragments, of greater than 50 or greater than 100 nucleotides in length; and that only sequences of at least 15 bases in length are disclosed. It is further alleged that there is no support in the specification for polynucleotides of 98% or 99% homology to the disclosed sequences or fragments thereof.

Applicants point out, however, that the specification discloses GDF-16 polynucleotides comprising "at least 15 bases" (page 7, lines 18-21). As such, it is submitted that skilled in the art would have known that a polynucleotide of the invention can have a length between 15 nucleotides and the full length of a GDF-16 polynucleotide, including, for example, a sequence of greater than 50 bases in length, or a sequence of greater than 100 bases in length, and, therefore, that one skilled in the art, viewing the specification, would have known that Applicants were in possession of the claimed polynucleotides. Nevertheless, in order to advance prosecution of the subject application, claims 43 and 47 to 52 have been cancelled. Accordingly, it is submitted that this rejection is moot.

The rejection of claims 43, 51 and 52 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification is respectfully traversed.

It is stated in the Office Action that one skilled in the art, viewing the subject application, would not have concluded that Applicants were in possession of GDF-16 polynucleotide sequences comprising fragments that were not required to have any particular function. Although Applicants traverse this rejection, it is noted that claims 43, 51 and 52 have been cancelled herein to advance prosecution of the subject application. Accordingly, it is respectfully submitted that this rejection is moot.

The rejection of claims 43, 47, 51 and 52 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite is respectfully traversed.

It is stated that the term "biological activity" is not defined in the specification and, therefore, that one skilled in the art would not know what activity was intended. Although Applicants traverse this rejection, it is noted that claims 43, 47, 51 and 52 have been cancelled herein to advance prosecution of the subject application. Accordingly, it is respectfully submitted that this rejection is moot.

#### **D. Objection to the Claims**

Claims 48 to 50 are objected to for the typographical error in the term "polynucleotide". Claims 48 to 50 have been cancelled and, therefore, it is submitted that the objection is moot.

In re Application of Lee et al.  
Application No.: 09/485,045  
Filed: May 12, 2000  
Page 7

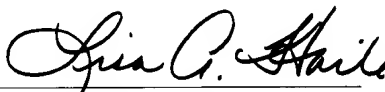
PATENT  
Attorney Docket No.: JHU1440-1

In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' representative if there are any questions relating to this application.

Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Date: February 18, 2003



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In re Application of Lee et al.  
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Filed: May 12, 2000  
Exhibit A - Page 1

PATENT  
Attorney Docket No.: JHU1440-1



**EXHIBIT A**

**MARKED VERSION OF CLAIMS SHOWING AMENMDENTS**

Claims 54 and 55 were amended as follows:

54. (Amended) An expression vector including the polynucleotide of claim [52] 53.
55. (Amended) A host cell stably transformed with the vector of claim [53] 54.

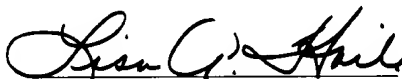
In re Application of Lee et al.  
Application No.: 09/485,045  
Filed: May 12, 2000  
Page 2

PATENT  
Attorney Docket No.: JHU1440-1

No fee is deemed necessary in connection with the filing of this paper. However, if a fee is required, the Commissioner is hereby authorized to charge any other required fees associated with the filing submitted herewith, or credit any overpayments to Deposit Account No. 50-1355. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

Date: February 18, 2003



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